European Science Methodical Journal
ISSN (E): 2938-3641
Volume 2, Issue 5, May - 2024

INHIBITION OF THE GROWTH OF E. COLI AND CANDIDA BY SILVER COMPLEXE (I) WITH LIGANDS

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Abstract:

This study is included synthesis and characterization of a number of complexes for Silver(I) ion, with molecular formula of the complexes: [{Ag(CAPR)(NO3). (H2O)} where: CAPR=Captopril. The complexe were prepared from silver nitrate with ligands 1:1 in 25 oC. The complexe were characterized by means of the the Ultraviolet visible spectrum UV, the flame atomic absorption, And the CHN analysis, This complexe were studied for their effect against some species of bacteria and fungi. The study showed that the complex {Ag(CAPR)NO3H2O} had the inhibitory ratio to bacteria and fungi.

Keywords: Silver Nitrate with Ligands, (FT-IR), UV, Bacteria and Fungi.

Introduction

There is a set of unique chemicals, physical and medicinal properties of silver complexes. These properties attracted the attention of researchers, making them the subject of a study for many issues related to fighting fungal and bacterial infections [1, 2]. The importance of silver complexes lies in the fact that they are considered effective, but with low toxicity, which makes them useful in topical treatments, especially in burns [3, 4]. This low toxicity repre-sents an extermination factor for various pathogens, whether viral, fungal or bacterial, and yet it is not harmful to humans [5,6]. Over the years, there are many experiments that have been conducted to find out the biological activity of various types of bacteria against silver com-plexes, and all of these experiments indicated that the reason for its activity is its unique structural bonds [7]. It is possible that these bonds form a specific coordination with a metal ion, especially those containing bonds On electron donor atoms, a comprehensive change in these bonds may occur due to chelation, as it often results in a synergistic effect of both the bond and the metal ion [8-12].

The Complexes are Containing Mixed Ligands

Many negatively charged complexes of tetra halogen and halogens divalent metal ions containing nitrogen and sulfur donor ligands were prepared in various ways. Complexes containing a mixture of antagonistic ligands of quaternary, pentameric, and hexagonal coordination, cobalt (II), nickel (II), and copper (II) ions, were also prepared) and cadmium

(II), and the nature of the central metal ion and ligand affects the number of coordination and oxidation solutions in the complex, as the complexes are negatively or positively charged [13]. Several studies have been conducted on silver complexes containing mixed ligands. The monomeric silver complexes with triple phosphenes have been extensively studied because of their effect on cancerous tumors and bacteria.

Captopril

Captopril is given orally, as it inhibits the enzyme angiotensin. It is widely used as an antihypertensive drug to reduce heart failure [14]. Pharmacologically active captopril is obtained from the drug Capoten. Captopril was developed in 1975 by three researchers at the American pharmaceutical company Squibb (now called Bristol). Myers Squibb) Onditti, Rubin, and Cushman. Squibb submitted the drug to the US Patent Organization in February 1976, and the organization approved this drug in September 1977. The chemical composition is as shown in Figure 1.

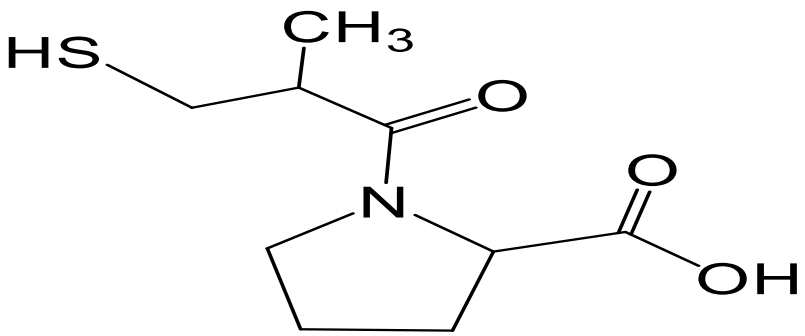

Figure 1. The structural formula of Captopril

Table 1. Some physical and chemical properties of the compound captopril

Captopril(CAPR)	
Systematic Name	1-[(2*S*)-3-mercapto-2-methyl propionyl]-*L*-proline
Molecular Formula	$C_9H_{15}NO_3S$
Molecular Weight	g/mol
Melting Point	°C104-103
K_a	3.7

Captopril has caused high toxicity when given in large doses to patients suffering from collagen vascular disease or renal failure. Minor toxic effects include skin allergies, rashes, and fever, which occur in up to 15% of patients who use the drug [15,16].

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MATERIALS AND METHODS

All assays for the experiment were carried out at SDI laboratory / Samarra, which included melting point detection, using 3-10 M solution of the sample in DMSO for the purpose of determining the molar electrical conductivity by using HI 9811-5 at room temperature.

A spectrophotometer was also used, In addition to using a spectrophotometer (UV-Vis), which provided the opportunity to know and measure the electronic spectra of the bonds. Within a range of (200-1000) nm, using a quartz cell of (1.0) cm long, with a concentration of 3-10 M of the sample in DMSO at room temperature. A commonly used technique for measuring the percentage of complexes is the flame atomic absorption spectroscopy of Shimadzu (A.A) - 680A to determine the Ag + ion in the complexes. Finally, the elemental microanalysis (CHN) of the complexes was detected using a EuroVector EA3000 elemental analyzer.

Synthesis of Silver(I) Complexes

Complexes: [Ag(L)(NO3) (H2O)]. H2O

Silver nitrate (1.00 mmoles) was dissolved in D.Water (10 ml). This solution was added to a solution of (L) (1.00 mmoles) in ethanolic (20 ml). And after the addition was complete the solution was heated to 50 ºC with stirring for 0.5 h, then left over night. Resulted a white precipitate, which were filtered, washed with cold ethanolic and dried in a desiccator over anhydrous CaCl2 [17].

Complex-1: [Ag(CAPR)(NO3).(H2O)]

This complex was prepared as in the first paragraph and according to the weights in Figure 2. and as follows:

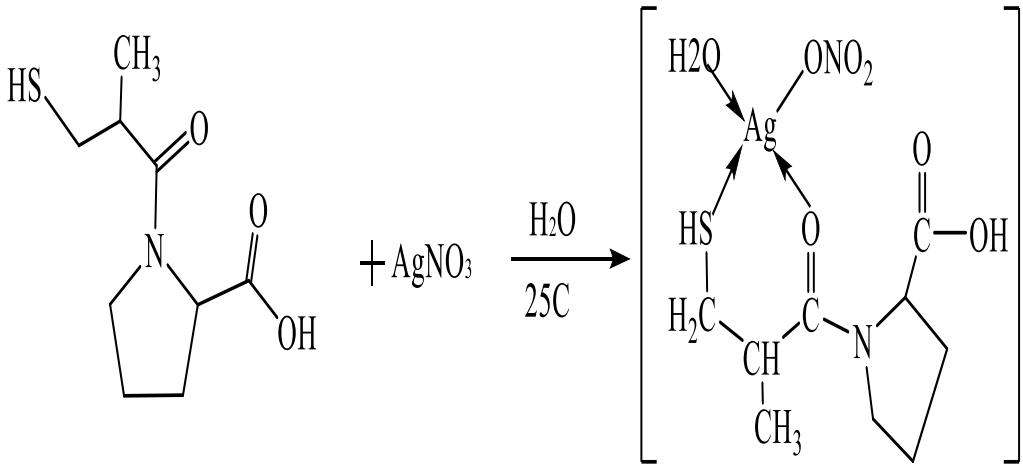

Figure 2. Synthesis route of complex-1: [Ag(CAPR)(NO3)(H2O)].

Bacterial and fungal isolates:

Pure bacterial isolates were obtained from the Microbiology Division / Central Laboratory Department / The State Company for the Manufacturing of Medicines and Medical Supplies – Samarra- Iraq , which consisted of two negative isolates Escherichia coli and Bacillus pumilus,

and two positive isolates Staphylococcos aureus and Micrococcus, and some fungi were used in this study Monelia and Candida albicanus.

Susceptibility testing:

The effectiveness of the prepared complexes on bacteria was chosen by the agar-well diffusion method, whereby 1.5ml of activated bacteria or fungi isolates were poured into the nutrient medium in a flask containing 250ml of the culture medium in its liquid state at a temperature of 40C˚, then stirred. To ensure complete contamination, it was poured into petri dishes at an amount of 18ml per dish and left to solidify at room temperature.

After solidification, holes were made in the dishes using the Cylinder metric method (according to the American Pharmacopoeia USP 35) with a cork borer, as 50µl of the chemical complex was placed in each hole of the holes, and the same amount of the other compound was placed in the corresponding hole, and so on. The plates were incubated in the incubator at a temperature of 37C˚ for 24 hours for bacteria, and at a temperature of 32C˚ for 48 hours for fungi, and the diameters of the zones of inhibition of microbial growth were measured by a Zone reader [18].

Statistical Analysis

The Statistical Analysis System- SAS (2012) was used to effect of different factors in study parameters. Least significant difference –LSD test was used to significant compare between means in this study [19].

RESULTS

The tetrahedral sp3 geometrical structure was suggested for prepared complexes based on the characterization data for all techniques.

Elemental microanalysis (C.H.N)

The elements in the complexes were estimated by microanalysis and flame absorption spectrometry as shown in Table :(3)

Table 3. estimate the percentage of the practical and theoretical elements of the prepared complexes

Seq	Complexes	Found(cal.)%					
		C	H	N	S	O	Ag
1	[Ag(CAPR)(NO3).(H2O)]	(24.34) 25.54	(4.12) 4.52	(6.66) 6.61	(7.85) 7.57	(31.48) 30.24	(24.87) 25.54

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Table 4. Diameter of inhibition of the complexes for the growth of some types of bacteria and fungi in (mm)

N	Captopril		
	10mg/ml	**25mg/ml**	**50mg/ml**
E.c	18.6	19.4	**20.2**
B.p	9.9	11	**12.6**
M.i	27	30	**34**
S.a	10.8	11.4	**12.2**
C.a	25	29	**34**
M.a	23	26	**28**

Effect {Ag(CAPR)NO3} on bacteria and fungi under study

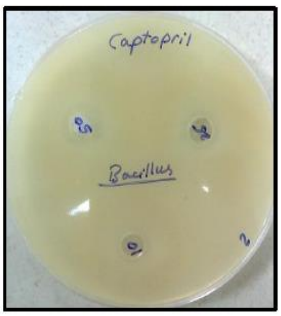


Figure 3. The activity of complex (1) against Bacillus pumilus, showing the concentrations in mg/ml.

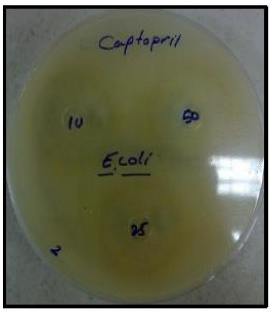
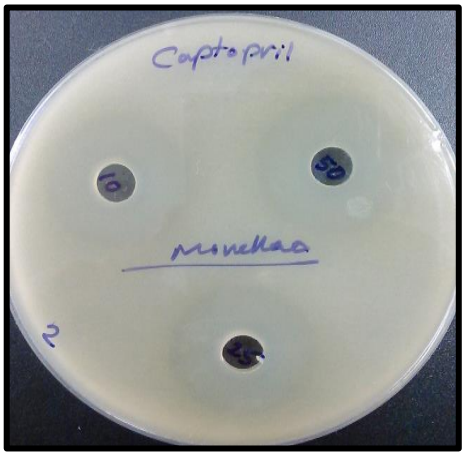
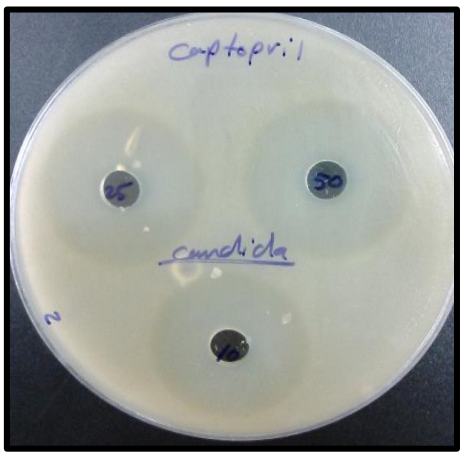


Figure 4. The activity of complex (1) against E.coli bacteria, showing the concentrations in mg/ml

Figure 5. The activity of complex (1) against Staph. aureus, showing the concentrations in mg/ml.

Figure 6. The activity of complex (1) against Micrococcus bacteria, showing the concentrations in mg/ml.





DISCUSSIONS

Studies have shown that silver ions interact with sulfahydryl (SH-) for groups of proteins as well as DNA bases, which leads to the inhibition of respiratory bacteria. Inhibition may occur through damage to the bacterial cell membrane, as it can attack the lipids in the membrane and then lead to the collapse of the membrane function [20]. The complexes may surround the bacterial cell, preventing the entry of basic materials that the yeasts need, leading to their death [21]. Another possibility is that the materials resist the microorganisms in releasing silver ions in response to the surrounding humidity. Silver ions have been proven to interact with proteins

by binding to the phosphate bonds with the protons. The membrane of bacteria results in a gradual collapse of the membrane proton, which causes the disruption of many cellular metabolic mechanisms and thus cell death.

CONCLUSIONS

It is expected that it is able to penetrate into the bacteria and cause more damage, and it is possible that it binds to the bacterial DNA and leads to its inactivation and preventing its replication. Silver complexes are more beneficial than organic materials alone because they are characterized by a higher degree of thermal stability and less toxicity to non-target organisms. Than typical organic chemicals, it has a higher level of resistance to ultraviolet (UV) radiation.

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